Technical Abstract for: Oncocidex Protocol ON-02 entitled "A Phase I Study of the Treatment of Recurrent or Progressive Malignant Glioma Using Expanded Autologous Bone Marrow-Derived Stromal Cells Non-Virally Transduced to Express IL-12 (BMSC-12)

Glioblastoma multiforme is a highly malignant form of glioma (primary brain tumor) that is among the leading causes of cancer mortality in people under 54 years of age. Due to its expansive and infiltrative nature, it is nearly impossible to completely extirpate the tumor, which results in tumor recurrence in 80% of all patients. Unfortunately, current therapies to treat the recurrence, such as local radiation, chemotherapy and surgical removal have not proven effective. BMSC-12 has been developed in order to address the problem at the biological level.

BMSC-12 utilizes autologous bone marrow stromal cells which have been non-virally transduced with mammalian expression vector (MEV) to express IL-12. BMSCs, when directly transplanted in the brain, have been shown to migrate towards sites of injury or disease in the CNS. IL-12 is a powerful cytokine with potent anti-tumor activity, dependent on IFN? secreted by Th-1 or NK cells, enhancement of CD8+ T lymphocytes, induction of CD3+ NK cells and the activation of tumor-infiltrating lymphocytes.

Data from pre-clinical studies demonstrates the safety (represented by a lack of adverse events) of high dose administration of IL-12 (virally) transduced BMSCs in a rat glioma model at doses 10 times higher than what will be used in this study. In addition, there are 2 additional studies currently ongoing, the first a 13 week study of the tumorgenicity of non transduced huBMSCs in athymic mice and the other a safety study of single repeated dose IL-12 secreting BMS cells after electroploration in normal and glioma rat models. Half of the animals in the tumorgenicity study were sacrificed at 21 days and no tumor formation as a result of the BMSCs was noted. Day 96 results are pending. Results from the repeated dose study are pending and should be available in mid October.

After obtaining informed consent, BMSCs will be harvested from the subject and the cells will be expanded and transduced with IL-12 via MaxCyte's electroporation method. BMSC-12 will then be administered either through stereotactic injection or through an existing intracranial catheter into 1 subject with recurrent or progressive malignant glioma who has received maximum conventional therapy. It is believed that the BMSC-12 will migrate locally to any remaining tumor cells, releasing interleukin-12 at the cellular level, and causing the induction of macrophages, NK cells and T-lymphocytes with resultant tumor cell death. Based on pre-clinical experience of BMSC expression, 10 million cells will provide approximately 4,000 to 5,000 ng of IL-12 over the 72-96 hours following administration. Repeated monthly administrations will be given as tolerated in doses of 10 million cells for up to 10 repetitions. Clinical benefit may include delayed or no tumor progression or even tumor regression or destruction. Systemic side effects are expected to be minimal.

The primary study endpoint is safety as defined by a lack of significant adverse events related to the BMSC-12 or BMSC-12 administration. Other measures that will be followed are the following: changes in Karnofsky performance scale as compared to Baseline; time to disease progression as evidenced by MRI calculated from Baseline and survival measured as length of survival calculated from Baseline.

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